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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/823,850	03/30/2001	Trey E. Ideker	P-IS 4588	7007
23601	7590	01/31/2005	EXAMINER	
CAMPBELL & FLORES LLP 4370 LA JOLLA VILLAGE DRIVE 7TH FLOOR SAN DIEGO, CA 92122			MARSCHEL, ARDIN H	
			ART UNIT	PAPER NUMBER
			1631	

DATE MAILED: 01/31/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/823,850	Applicant(s) IDEKER ET AL.	
	Examiner Ardin Marschel	Art Unit 1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 04 May 2004 and 09 July 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-85 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-85 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 04 May 2004 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|--|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input checked="" type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. (<u>2 copies</u>) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____. | 6) <input type="checkbox"/> Other: _____. |

DETAILED ACTION

Applicants' arguments, filed 5/4/04 and 7/9/04, have been fully considered and they are deemed to be persuasive to overcome previous rejections and objections of record. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. Unfortunately, upon reconsideration, the following rejections and/or objections are newly applied. They constitute the complete set presently being applied to the instant application.

Applicants have fully met their burden to respond to the Final office action, mailed 1/29/04, as of submissions, filed 5/4/04 and 7/9/04. However, due to newly found issues as summarized below the Finality of the Office action, mailed 1/29/04, is hereby withdrawn. Also, due to this reopening of prosecution, the Notice of Appeal, filed 7/29/04, is deemed moot.

Applicants' Interview of 1/26/05 is acknowledged to approve entry of an Examiner's amendments to overcome newly found unclarities. Since there are other significant issues, as summarized below, regarding the instant claims such an Examiner's amendment is not presently provided for.

VAGUENESS AND INDEFINITENESS

Claims 1-85 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 22, lines 1-2, cites "said univariate distribution" and depends from claim 1. There is no clear antecedent basis for such a distribution either in claim 22 or 1 which

thus causes claim 22 to be vague and indefinite as to what is meant by "said univariate distribution". Claim 21 cites such a distribution. Clarification via clearer claim wording is requested.

Claim 40, lines 1-2, cites "said parametric distribution" and depends from claim 38. There is no clear antecedent basis for such a distribution either in claim 40 or 38 which thus causes claim 40 to be vague and indefinite as to what is meant by "said parametric distribution". Claim 39 cites such a distribution. Clarification via clearer claim wording is requested.

Claim 1, part (b), cites the observed signal as being related to a mean signal by an additive and multiplicative error. The claim is vague and indefinite as to what relatedness is meant, especially because the intent of the claim in line 1 is the determining of what reasonably is a quantitative value of a true signal. Such quantitation is indicative of some type of quantitative relatedness which reasonably requires some type of computation of a true signal value which confusingly is not set forth in claim 1. Thus, the metes and bounds of the relatedness regarding signal determination either as the true signal or related to the observed signal are unclear. Clarification via clearer claim wording is requested. Claims dependent from claim 1 also contain this unclarity due to failing to set forth some type of computational relatedness to specify what determining is performed. It is noted that claim 4 cites a formula relationship regarding these parameters with the exception of relating the true signal thereto in order to define the metes and bounds of the determining of lines 1-2 of claim 1 and therefore fails to prevent this unclarity as to metes and bounds of relatednesses

as described above. Claim 8 similarly contains this unclear relatedness issue due to citing signal means without defining what relatedness to the true signal is meant thereby. Independent claims 18, 34, 52, 71, 83, and 85 also contain this unclarity and corresponding claims dependent therefore as compared to claims dependent from claim 1. See, for example, claims 20, 37, 54, and 73 which is additionally unclear for the same issue as described above for claim 4.

Claim 1, line 6, indicates "said analyte" whereas lines 3-4, cite "one or more analytes". Thus, the antecedent basis for the singular "said analyte" in lines 3-4 is unclear wherein both singular and plural analytes are cited in lines 3-4. This issue is also present in independent claim 18 and claims dependent therefrom due to their dependence. Clarification via clearer claim wording is requested.

Claim 1, part (a), cites the measuring of "an observed signal" whereas part (b) determines a "mean signal" in its first line. The antecedent basis for a "mean signal" is unclear as there are no multiple signals cited previous to the first line of part (b) of claim 1 from which to determine a "mean". This issue is also present in independent claims 18, 34, 52, 71, 83, and 85 and claims dependent therefrom due to their dependence because claims 18 etc. do not provide antecedent basis as to plural signals regarding a "mean signal" calculation, however, sample pairs are cited but not what signals are averaged to determine the mean signal in part (b) thereof. Clarification via clearer claim wording is requested.

Claim 14, line 2, cites a "said enhanced values" which lacks clear antecedent basis. Clarification via clearer claim wording is requested.

Independent claims 1, 18, 34, 52, 71, 83, and 85 all cite preambles with determinations such as "true signal" or "relative amounts" which are not calculated or determined in actual claim steps beyond the preamble. Thus, these claims and those dependent therefrom are vague and indefinite as to whether the respective preambles or the actual claim steps control the metes and bounds of the claims. Clarification via clearer claim wording is requested.

PRIOR ART

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1, 3, 5, 6, 11, 13, 22, 34, 36, 38, 39,, 44, and 46 are rejected under 35 U.S.C. 102(e)(2) as being clearly anticipated by Stoughton et al. (P/N 6,351,712).

Stoughton et al. summarizes the combining of expression profiles via statistics in the title and abstract. The abstract further describes the calculating of individual errors optionally coupled with rank methods to determine a probability that a cellular component is up or down regulated. Averaging of expression levels is also described in the abstract thus documenting the same type of subject matter regarding analyte signal determination with error calculation in order to obtain a probability likelihood of an

observed signal being indicative of a cellular response. In particular columns 15-17 of the reference disclose averaging protocols with weighting regarding repeated measurements to yield an expression level which reasonably is a true signal as required in the first two lines of instant claim 1. The measuring of observed signal in a microarray experiment via fluorophores is cited in column 15, line 49, through column 16, line 10, with determining an error envelope. The analytes measured via fluorophores are mRNAs etc. as generally described in columns 1-2 of Stoughton et al. These disclosures anticipate part (a) of instant claim 1. Part (b) of instant claim 1 is anticipated in column 15, line 49, through column 16, line 31, wherein the fluorophore intensity signals, as observed, are related to a mean signal via equation (8) therein and intensity contour lines are fitted in accordance with equation (7). Equation (7) is described in column 14, lines 4-59, wherein additive and multiplicative errors are combined as specifically described in column 14, lines 20-43, regarding said intensity values. Several example calculations are then disclosed in columns 16-31 to more fully illustrate the determination of probability of cellular constituent up or down regulation as noted above as the intent of the disclosure of Stoughton et al. in the abstract. In column 14, lines 30-43, the parameters " $\sigma_{X \text{ or } Y}$ " squared represent additive errors and are independently formulated from parameter "f" which is the multiplicative error as also required in instant claim 3. These parameters are singularly defined and thus anticipate the univariate distribution and parametric limitations in instant claims 5, 6, and 22. The signals and error determinations all are derived at the same time as the fluorophore measurements and determine a mean signal thus also anticipating instant claims 11

and 13. The error calculations and probability of expression profiles determinations as described above reasonably produce enhanced values for a probability likelihood of such determinations as in claim 34 thus also supporting rejection of claim 34 hereunder as well as dependent claims from claim 34 which cite the same dependent limitations as corresponding claims which are dependent from instant claim 1.

No claim is allowed.

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the Central PTO Fax Center. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CFR § 1.6(d)). The Central PTO Fax Center number is (571) 273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ardin Marschel, Ph.D., AU 1631 Supervisory Patent Examiner, whose telephone number is (571) 272-0718. The examiner can normally be reached on Monday-Friday from 8 A.M. to 4 P.M.

Any inquiry of a general nature or relating to the status of this application should be directed to Legal Instrument Examiner, Tina Plunkett, whose telephone number is (571) 272-0549.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

January 28, 2005

Ardin H. Marschel 1/28/05
ARDIN H. MARSCHEL
SUPERVISORY PATENT EXAMINER